1: J Neuroimmunol. 2003 Dec;145(1-2):77-85. Links

Via beta-adrenoceptors, stimulation of extrasplenic sympathetic nerve fibers inhibits lipopolysaccharide-induced TNF secretion in perfused rat spleen.

Kees MG, Pongratz G, Kees F, Scholmerich J, Straub RH.

Laboratory of Neuro/Endocrino/Immunology, Department of Internal Medicine I, University Hospital, Regensberg 93042, Germany.

Using a spleen slice microsuperfusion technique in mice, we have previously characterized the role of norepinephrine (NE) and other neurotransmitters for sympathetic modulation of IL-6 and TNF secretion of splenic macrophages. Since experiments in spleen slices do not reflect the situation of an entire perfused organ, we investigated sympathetic modulation of lipopolysaccharide (LPS)-induced secretion of IL-6 and TNF in perfusion experiments of rat spleen. In an organ bath, perfusion was performed in explanted whole spleens, and catecholamines and cytokines were measured by HPLC and ELISA, respectively. Release of NE depended on stimulation frequency (maximum at 10 Hz). Apart from NE, perfusates also contained significant amounts of dopamine and epinephrine. Furthermore, perfusate epinephrine levels correlated positively with perfusate NE levels (RRank=0.750, p<0.001) but not with plasma epinephrine concentrations. This indicates that epinephrine is a conversion product of sympathetically released NE. Early electrical stimulation of extrasplenic splenic nerves, 20 min after administration of LPS, significantly inhibited TNF secretion. This electrically induced effect was abrogated by simultaneous administration of propranolol (10(-6) M) but it was not influenced by administration of either an alpha1- or alpha2-adrenergic antagonist. Late electrical stimulation of splenic nerves, 2.5 h after administration of LPS, did not change TNF secretion. Interestingly, no influence of early or late sympathetic nerve fiber stimulation on IL-6 secretion was observed. In conclusion, this is the first perfusion study of the entire spleen that demonstrates that early electrical stimulation of sympathetic splenic nerve fibers directly inhibits LPS-induced TNF secretion. This study corroborates the idea that splenic sympathetic nerves are able to inhibit important activators of the innate immune system when stimulation happens very early or even prior to their induction by LPS.

PMID: 14644033 [PubMed - indexed for MEDLINE]

Display AbstractPlus Show 20 Sort by Send to